The objection to the drawings has been noted. New formal drawings will be filed when the application is allowed.

Claims 9, 30, 34 and 45 have been amended to correct the peptide formulas in the claims so that they correspond to the specification. SEQ ID NO: 41 has been reviewed and it is believed to correct. For these reasons, it is requested that this ground of objection be withdrawn.

Claims 1-53 were rejected under 35 U.S.C.§112, second paragraph for failing to particularly point out and distinctly claim the subject matter that the applicant regards as the invention.

Reconsideration is requested.

Claims 1 and 2 were noted as being indefinite in the use of the terms "of the formula" and "having". By this Amendment, these terms have been replaced by the term --comprising-- in order to adopt the Examiner's suggestion. The peptide of Claim 11 corresponds to the ABC formula of claim 1. The peptides of claims 17-50 all meet either the A, AB or ABC formula of claim 1 because they contain the amino acids that are defined in those formulas. For these reasons, it is requested that this ground of rejection be withdrawn.

Claims 1-34 and 51 were rejected under 35 U.S.C.§102(b) as being anticipated by Porro (WO/95/03327).

Reconsideration is requested.

The Porro reference describes peptides that are used in the present invention. The direction to make vaccines appears at page 7, lines 14-20 of the Porro reference. Those directions recite the use of "stoichiometric amounts of Lipid-A or LPS and the peptides. Claim 1 of the present application defines a novel process of making a vaccine over the teachings of Porro in that the text of claim 1 points out that "a stoichiometric" excess of the peptides is used with the LPS to make the vaccine of the invention. This concept is not disclosed by the Porro

reference and for this reason, Porro does not anticipate the claims of the present application.

Claims 1-51 and 53 were rejected under 35 U.S.C.§103(a) as being obvious over Hancock et al. or Velucchi et al. in view of Porro.

Reconsideration is requested.

The present invention provides a vaccine which is a specific complex of LPS and the peptides described in the above identified application. The Hancock patent is silent as to the preparation or use of any material as a vaccine.

Hancock discloses a cationic peptide having anti-microbial activity and LPS-binding activity which are used for suppressing the growth of bacteria and the treatment of endotoxemia-associated disorders. At col.8, line 23 to col.10, line 15, Hancock lists a plurality of uses for the peptides that are described. These uses involve bactericidal uses of the peptides, treatment of septic shock, coadministration with an inhibitor of TNF or an antibiotic. There is no disclosure of the therapeutic coadministration of a peptide-LPS complex which is made from an excess of peptide. Hancock failed to recognize that the formation of a complex of a peptide and LPS would provide a complex that would have antigenic properties which would allow its use as a vaccine to prevent gram-negative infections and the effects of endotoxin. Table 5 at col. 20 of Hancock discloses various affinity constants for LPS and two of the Hancock peptides but contains no suggestion that an excess of peptide could be added to LPS to produce a useful vaccine. The usefulness of a material as a vaccine depends on its lack of toxicity and this could not have been predicted from the teachings of Hancock who fails to teach the use of a complex of the peptide and LPS for any purpose. For this reason, Hancock fails as a teaching reference.

Velucchi et al is the applicant's own publication which was published less than one year prior to the filing date of the present application. As evidence of the fact

that Velucchi et al. is the publication of the present applicant, attached hereto is a declaration which unequivocally attests to this fact. For this reason, Velucchi et al. should be not be applied to reject the claims of the present application.

The Porro patent has been distinguished supra as not suggesting a vaccine made with a excess of a peptide according to the claims of the present application and LPS. Fig. 1 of the present application includes comparative data which shows that when a complex having a ratio of 1:25 of LPS to peptide and a complex having a ratio of 1:250 of LPS to peptide are assayed by their ability to inhibit TNF production induced by LPS N.meningitidis A1, the higher ratio of peptide is about seven times more effective in suppressing TNF production. This data shows the effect of increasing the ratio of peptide to LPS in making a vaccine according to the applicant's invention. These results show the efficacy of the concept of using more than a stoichiometric amount of peptide to LPS in making a vaccine. For these reasons, it is requested that this ground of rejection be withdrawn.

Claim 52 is patentable for the same reasons set forth in response to the rejection of claims 1-51 and 53. The Immunization Practices Advisory Committee does not disclose any vaccines for use in protecting a host against endotoxins and the recommendation to coadminister different vaccines does not make obvious the use of the vaccine of the present invention with other vaccines. At page 844, the Advisory Committee cautioned that vaccines associated with local or systemic side effects are given simultaneously, side effects may be accentuated and "these vaccines should be given separately". This does not make the subject matter of claim 52 obvious. New claim 54 points out a preferred stoichiometric ratio of LPS:peptide that is disclosed in the specification at page 6, line 28. This claim is patentable for the reasons set forth supra.

An early and favorable action is earnestly solicited.

Authorization is givfen to charge any additional fee to Deposit Account No. 08-1540.

Respectfully submitted,

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner for Patents, Washington, D.C. 20231, on 1-5-00